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FATAL COMPLICATIONS FOLLOWING USE OF POTASSIUM PERCHLORATE IN THYROTOXICOSIS

REPORT OF TWO CASES AND A REVIEW OF THE LITERATURE

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ABSTRACT

Five cases of complications due to potassium perchlorate are reported. Two of the cases were fatal and are described in detail. A comparison of our experience with propylthiouracil and perchlorate is presented. In our opinion the results do not justify the continued use of perchlorate in the therapy of thyrotoxicosis.

Perchlorate has been in use since 1954. Following the experimental work of Wyngaarden et al. (1, 2), Kraatz et al. in Germany (3) and Morgans and Trotter in England (4) reported the results of the treatment of thyrotoxicosis with doses of 0.4 g daily. These authors listed nausea, rash and leukopenia as the most frequent side effects, but found no serious complications, and recommended perchlorate as the best available drug. Godley and Stanbury (5) reported the results of treatment in 24 patients with no serious complications. They mentioned skin rash, gastrointestinal disturbances, leukopenia, loss of hair and proteinuria as side effects. Further reports by Morgans and Trotter in 1957 (6) and Smellie (7) again confirmed the low toxicity of the drug. In 1960 reports by Crooks and Wayne (8) and Morgans and Trotter (9) described the increased incidence of complications with the larger doses then being used (1.6 g daily). No fatal complications were reported, although some cases of agranulocytosis did occur.

Since then, several cases of agranulocytosis, none of them fatal, have been described (9–14) with doses ranging from 1 to 1.6 g daily.

Cases of fatal aplastic anemia were first reported in 1961 by Hobson (10) in a woman receiving 0.6 to 0.8 g daily for 33 weeks, and by Johnson and Moore (15) in a woman treated for three months with doses of 1 g daily, followed by 0.2 g daily. Fawcett and Clark (16) reported a case of fatal aplastic anemia in a woman treated for six months with doses of perchlorate ranging from 0.4 to 0.6 g daily. Two similar cases were reported by Krevans et al. (17) in a woman receiving 0.8 g daily intermittently for two months, and by Gjemdal (18) in a woman receiving 0.4 to 0.6 g daily.

Nevertheless the use of perchlorate in many centers in Europe and Israel has been continued, mainly because of the possibility of using it for long periods and its easy use in children. In a relatively small group of cases we have seen severe reactions to perchlorate in five patients. The purpose of this paper is to

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describe two fatal cases and to comment on the use of perchlorate.

CASE REPORTS

Case 1. A 60-year-old woman was admitted to our department on 8 August 1963, with a history of fever, chills and pallor. The past history was noncontributory except for mild diabetes, which was treated by diet only. Two years before admission, thyrotoxicosis was suspected because of sweating, loss of weight and nervousness. This diagnosis was later confirmed by the presence of high basal metabolic rate (BMR) and protein-bound iodine values. She was treated as an outpatient with propylthiouracil and later with radioactive iodine; because response to this treatment was inadequate, she was started on potassium perchlorate, 1 g daily, two months before admission. Weekly blood counts were performed during treatment; the last white blood count before admission was 5,000/mm³.

Physical examination revealed a pale febrile woman, with slight bilateral exophthalmos, lid lag and slight redness of the throat; the blood pressure was 140/90 mm Hg. A soft systolic murmur was heard over the apex; the lungs were normal. The liver was enlarged and tender and palpable 5 cm below the costal margin. There were several hemorrhagic pustulae present on both legs. Neurologic examination was normal.

On admission the hemoglobin (Hb) was 6 g%, white blood count 1,400/mm³, and the platelet count 20,000/mm³. Bleeding time was more than 30 min. Erythrocyte sedimentation rate (ESR) was 145 mm (Westergren) after one hr. Blood urea and liver function tests were normal. Blood cultures were sterile and urine examination normal.

The patient's fever remained high throughout her stay in hospital. Despite transfusions of fresh blood, antibiotics and steroids, her condition deteriorated. The leukocyte count dropped to 800/mm³ on the seventh day. Bone marrow smears showed complete lack of both erythropoiesis and granulocytopoiesis. The patient died on the tenth day after admission.

Case 2. A 56-year-old woman was admitted with high fever and sore throat. There was a history of cholelithiasis for five years, and moderate hypertension which had been treated from time to time with reserpine and chlorothiazide.

A few months before admission she was found to have lost weight (12 kg) and her BMR was +36%. She was put on potassium perchlorate, 1 g daily. Two days before admission she complained of sore throat. A white blood count showed leukopenia of 3,000/mm³. Perchlorate was stopped and antibiotics were given.

Physical examination was negative except for follicular tonsilitis, the ESR was 130 mm after one hr, blood pressure was 140/95 mm Hg. The blood urea, sugar, electrolyte and liver function tests were normal. Blood cultures were sterile. The leukocyte count on admission was 1,600 mm³ and the differential count showed lymphocytes only; the Hb was 13 g%, thrombocytes 250,000/mm³, reticulocytes 0.8%. The bone marrow smears showed complete absence of cells of the myeloid series. Erythropoiesis and thrombocyte formation appeared normal. There was a relative increase of plasma cells and reticulum cells. No leuko-agglutinins were found, even after incubation of the blood with perchlorate. Massive antibiotic treatment (penicillin, streptomycin and tetracycline), steroids and transfusions of fresh blood were of no avail and the patient died.

In addition to these two cases, there were two of agranulocytic angina and one of pancytopenia, with maturation arrest of the bone marrow, all of whom recovered. These patients all received potassium perchlorate in doses of no more than 1 g daily.

DISCUSSION

Because of the severe complications in the above five patients, we reviewed all our cases that had received treatment for thyrotoxicosis, in order to compare the side effects occurring after perchlorate with those after propylthiouracil, which has been used for many years.

Our series consists of 284 patients (Table 1). Of 208 patients receiving propylthiouracil, eight developed leukopenia which disappeared on stopping the treatment; no severe reactions were noted (the series is presumably too small to have observed the well-known serious reactions to propylthiouracil). Seventy-six patients received perchlorate, and in this group there were two fatal cases and three severe, though nonfatal reactions. In view of

TABLE 1. *Side effects of propylthiouracil and perchlorate*

Drug	*No. of patients*	*Leuko-penia*[a]	*Agranulo-cytosis*	*Aplastic anemia*	*Other*	*Total complica-tions*
Propylthiouracil	208	8	0	0	6	14
Perchlorate	76	2	3 (1 fatal)	1 (fatal)	4	10

[a] Less than 4,000 white cells/mm³.

TABLE 2. *Complications of propylthiouracil and perchlorate therapy in our series and in the literature*

	Summary of series reported in literature		*Our series*	
Drug	*Total complications* %	*Blood dyscrasias* %	*Total complications* %	*Blood dyscrasias* %
Perchlorate 0.6 to 1 g daily	2 to 3	1 to 2	13	7.9[a]
1 to 2 g daily	16 to 18	6 to 8	Doses above 1 g not given	
Propylthiouracil	2 to 5	0.5 to 1	6.7	3.8[b]

[a] Two cases of leukopenia, three of agranulocytosis and one of aplastic anemia in 76 cases.
[b] Eight cases of leukopenia, no cases of agranulocytosis and no cases of aplastic anemia in 208 cases.

the occurrence of five severe reactions in the series of 76 patients who received perchlorate for a relatively short time, it seems unjustified to continue the use of this drug. We have therefore reverted to propylthiouracil for those cases requiring drug treatment of thyrotoxicosis.

Table 2 shows the incidence of complications of propylthiouracil and perchlorate therapy in the literature (8, 9, 19, 20) and in our cases.

Our limited experience shows a much higher incidence of total complications and of blood dyscrasias following perchlorate administration (1 g daily) than is reported in the literature with this dosage.

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JACOB ZAHALON (1630–1693) ON RULES FOR PHYSICIANS

כד. לא ישהה תיקון ורפואת החולי ולא ימתין זמן.

24. He should not postpone the repair and cure of the disorder and he should not wait too long.

לג. יחשוב קושי וסכנת ענין הרפואה.

33. Let him be aware of the difficulties and dangers in the practice of medicine.

לו. ירפא החולי במהירות במתיקות וודאות בלי ספק.

36. He should treat the disease with swiftness, sweetness, sureness and without uncertainty.